# Expediting the Development, Availability, and Approval of Medical Products for Counterterrorism

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# FDA Centers with Regulatory Oversight for Medical Products

- Center for Biologics Evaluation and Research
- Center for Devices and Radiological Health
- Center for Drug Evaluation and Research
- Centers work with Office of Regulatory Affairs, which has key role in field activities, e.g., inspections
- Office of Counter-Terrorism Policy and Planning in the Office of the Commissioner coordinates cross-cutting counterterrorism policy issues

# CBER: Innovative Technology Advancing Public Health

- Protect and improve public and individual health in the US and, where feasible, globally
- Facilitate development, approval and access to safe and effective products and promising new technologies
- Stimulate and assist in more efficient development of new & innovative products for biologic, chemical and radiologic defense

# Biological Products Regulated by CBER

- Blood, blood components and derivatives
- Vaccines (preventive and therapeutic)
- Allergenics
- Cell and Gene Therapies
- Tissues
- Xenotransplantation
- Related Devices (including certain IVDs)

# CBER Counterterrorism Efforts

- Work with HHS, NIH, CDC, DoD to identify gaps in medical countermeasures.
- Facilitate development of products under IND
  - New smallpox vaccines
  - New anthrax vaccines (e.g., recombinant protective antigen, “rPA”)
  - Vaccinia Immune Globulin (VIGIVs approved)
  - Anthrax Immune Globulin
  - Botulinum Antitoxin

# CBER Counterterrorism Efforts (cont.)

- Expeditious product development supported by:
  - Highly interactive review of submissions (good communication with sponsors essential)
  - Innovative approaches to labeling product containers to expedite availability
  - Interagency groups focused on development of animal efficacy models
  - Development of new immunologic and potency assays to assess immune response and product potency

# Approaches to Speed Product Availability and Facilitate Licensure/Approval

- Early and frequent consultation between sponsor, end user (if different) and FDA.
- Availability for emergency use under IND or Emergency Use Authorization (EUA)
- Fast track
- Priority review
- Accelerated approval
- Approval under “Animal Rule”
- Careful attention to risk/benefit and risk management issues

# Early and Frequent Consultation

- Improves communication process
- Improves quality of laboratory and clinical studies
- Reduces misunderstandings and likelihood of multiple review cycles
- Improves efficiency of product development
- Very resource intensive: CBER teams for priority counterterrorism product development/review (e.g., smallpox, anthrax vaccines)

# Product Availability under IND

- Facilitated implementation of protocols to use products under IND in an emergency (e.g., smallpox or anthrax release)
  - "Streamlined" IND
  - Informed consent required per regulations
  - Potentially cumbersome for widespread use
- Project BioShield allows for use of unapproved products or unapproved uses of approved products under EUA in specified circumstances

# Emergency Use Authorization (EUA): for Medical Products

- Sec. of HHS can declare emergency after Sec. of Defense, Homeland Security, or HHS determines an emergency (or potential for) exists
- Sec. of HHS can authorize use of product if
  - For serious or life-threatening condition
  - No adequate, approved, available alternative
  - May be effective
  - Known & potential benefits outweigh known & potential risks
- EUA granted for up to 1 yr, or until termination of declaration or revocation; can be renewed

# EUA: Conditions of Authorization

- Inform health care workers or recipients, if feasible
  - Product authorized for emergency use
  - Significant known & potential risks and benefits, extent to which unknown
  - Alternatives
  - Option to accept or refuse product
- Appropriate conditions for monitoring and reporting AEs, record keeping and reporting
- Authority for additional conditions, e.g., who may distribute or administer, collection and analysis of info

# EUA – Tracking and Review

- CBER has implemented a tracking system for pre-EUAs and EUAs
- FDA Draft Guidance for Industry: Emergency Use Authorization of Medical Products – in finalization stages

# Fast Track

- Product must be for serious or life-threatening condition and demonstrate potential to address unmet medical need
- Fast track designation applies to development program for specific indication, is granted during IND process
- FDA will consider the marketing application for priority review based on preliminary evaluation of clinical data
- If priority review granted, allows for rolling submission of marketing application

# Priority Review of Marketing Application

- Product eligible if provides significant improvement
  - In safety or effectiveness of treatment, diagnosis, or prevention of serious or life-threatening disease (CBER)
  - Compared to marketed products in treatment, diagnosis, or prevention of disease (CDER)
- Complete review of marketing application in 6 months
- Most counterterrorism products expected to qualify

# Accelerated Approval

- Product eligible if provides meaningful therapeutic benefit over existing treatments for serious or life-threatening illness
- Efficacy based on surrogate endpoint reasonably likely to predict clinical benefit
- Confirmatory post-marketing studies to verify clinical benefit
  - Usually underway at time of approval
  - Adequate and well controlled
- Withdrawal possible, e.g., benefits not verified

# Recent examples – Vaccinia Immune Globulin (VIG) Products

- Two VIG products under priority review licensed in 2005 (February and May)
- For treatment of certain serious complications of smallpox vaccination
- Accelerated approval based on serum neutralizing antibody level to vaccinia
- Post-marketing commitments to verify clinical benefit

# "Animal Rule"

- Products to reduce or prevent serious or life-threatening conditions caused by exposure to lethal or permanently disabling toxic chemical, biological, radiological, or nuclear substances
- Human efficacy studies not feasible or ethical
- Use of animal efficacy data scientifically appropriate
- Not applicable if approval can be based on efficacy standards described elsewhere in FDA regulations

# Animal Rule (cont.)

- Still need human clinical data
  - PK/immunogenicity data
  - Safety data
- Approval subject to post-marketing studies and any needed restrictions on use
- Potential limitations
  - No valid animal model of disease
  - How to predictably bridge animal data to humans
  - Confidence may be an issue, even with valid models

# Risk/Benefit for Counterterrorism Products

- FDA assesses risk/benefit for each product/use
  - Treatment: for otherwise untreatable, serious illness, reasonable to tolerate significant risk
  - Prevention: if given to well individuals, balance shifts, especially if pre-exposure
- Lack of efficacy can be a safety issue
  - Something is not always better than nothing
  - Ineffective therapy can inhibit development of effective therapies
- All such products need objective and effective risk communication

# Regulation of Counterterrorism Products: what is value added?

- As for other medical products, need consistent and objective protection of public health
- Attack with biological, chemical, radiological, or nuclear agents unpredictable
- Public expects safe and effective products, especially vaccines and other products given to well individuals
- Preserving confidence in medical products, and in public health leadership, is critical

# Thanks!

- We welcome your input and ideas...
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